REMARKS

Reconsideration of this application is requested.

The pending claims remain claims 1-27.

The Examiner is requested to reconsider the Section 112, 2nd ¶ rejection of claims 4, 5 and 27 in view of the amendments made to these claims. The applicant really does not believe the terms "substantially free of" and "substantially increases" are indefinite or otherwise unclear or uncertain as to scope. Nevertheless, claims 4, 5 and 27 have been amended to functionally underscore the intent of the language questioned by the Examiner. It is believed that these changes in claims 4, 5 and 27 obviate the basis for the Examiner's objection to the indicated claim language. Accordingly, withdrawal of the Section 112, 2nd ¶ rejection of claims 4, 5 and 27 is thought to be in order and is respectfully requested.

The Examiner is also requested to reconsider the Section 112, 2nd ¶ rejection of claims 1-27 in view of the amendments made to claim 1. The language used in amending claim 1 is thought to be consistent with the reasoning behind the Examiner's suggestions for amendment although the language applicant has employed is somewhat different. In any case, withdrawal of the Section 112 rejection of claims 1-27 is thought to be in order and is requested.

The Examiner is also requested, particularly in view of the amendments to claim 1, to reconsider the new Section 102(b) and Section 103(a) rejections as set out in Sections 12-18 of the action. With respect, it is submitted that the applicant's invention as defined in claims 1-27, as amended, is not disclosed by Bambara et al. (hereafter "Bambara") or obvious therefrom even if considered with the Examiner's secondary references.

As the Examiner will appreciate, the applicant's invention comprises binding an oligonucleotide to a titratable anion exchange composition at a first pH, passing a solution having an increasing pH gradient through the composition and eluting the oligonucleotide at a higher pH. It is this increase in the pH which causes the target oligonucleotide to elute.

The Examiner cites two examples of Bambara allegedly disclosing a process accoriding to the claims of the present invention. The first of these is the separation of urea from the primer referred to in the first full paragraph, second column of page 4608. Bambara here discloses removing the primer from the PEI-cellulose plate by using 2M

triethylamine bicarbonate buffer at pH 8.5. This solution, comprising the primer and residual urea from the previous stage is then loaded on to a DEAE-cellulose column. The pH of the solution at which the primer is loaded onto the column is therefore 8.5. The urea impurity is removed by passing through a solution having a pH of 7.5 – a lower pH than that used to load the sample onto the column, and finally the primer is eluted by use of the same pH 8.5 solution originally used to load the sample. This is therefore not a disclosure of loading a target oligonucleotide onto an anion exchange composition at a first pH, followed by passing a solution with an increasing pH through the composition to elute the target oligonculeotide. This first example of Bambara, therefore, does not anticipate the applicant's invention as the reference example does not disclose each and every feature of the claims of applicant's claim 1.

The second Bambara example cited by the Examiner is the separation of the primer from failed primers also in the first full paragraph, second column of page 4608. With respect, the applicant submits that the Examiner's assertion that this second example consists of binding in a neutral solvent followed by elution of the primer using a solvent with a pH of 8.5 is not a correct representation of the actual separation process disclosed by Bambara. Here, Bambara separates the primer from the impurity by plate chromatography using only the neutral solution. This can clearly be seen by Bambara's reference to "purified to single band homogeneity". The primer is then physically scraped off the plate. Clearly, the primer is separated from the failed primer impurities by plate chromatography using a single, fixed pH solution. There is no disclosure of the use of a solution with a pH increasing over time, such that the impurity elutes at a different pH from the target. This second example therefore does not anticipate the applicant's claims as it does not disclose each and every feature of the claims, particularly claim 1.

Consistent with the foregoing, the applicant submits that the Section 102(b) rejection based on Bambara should be withdrawn. Detailed comment on distinctions between applicant's dependent claims (claims 2-27) and Bambara are not thought to be necessary since applicant's main claim 1 is not anticipated by Bambara for the reasons noted.

With regard to the Examiner's Section 103(a) rejections, the applicant notes that Bambara and the secondary references do not make the applicant's invention, as defined by the amended claims, obvious. There is clearly no teaching in the Examiner's

references that would cause one of ordinary skill in the art to contemplate or reach the method of the present invention. In fact, Bambara goes to great lengths to avoid the use of an increasing pH gradient to separate target oligonucleotides, including using physical removal of bands of purified material from chromatography plates. Thus, Bambara, if anything, leads away from the applicant's invention.

In brief, the applicant submits that the present claims define a method which is not obvious from the teaching of Bambara, either alone, or in combination with any other of the documents cited by the Examiner.

Accordingly, withdrawal of the Section 103(a) rejection, along with the Section 102(b) rejection, is requested.

The application, as amended, is thought to be allowable and such action is respectfully requested.

Respectfully submitted,

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